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wherein said antibody or said active fragment does not immunoreact with a non-human, non-mouse or non-C. elegans eukaryotic eEF-2 kinase; and,

B. a pharmaceutically acceptable carrier.

REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated November 12, 2003.

Status of the Claims

Claims 51-59 are pending in the application. Claims 51, 52, 53, 54, 55, 57, 58 and 59 have been amended. Support for the amended claims can be found generally through Applicants' specification.

The §102 Rejection

The Examiner has maintained her rejection of Claims 51 and 52 under 35 U.S.C. § 102(b) as unpatentable over Redpath et al. [J. Biol. Chem. 1996, Vol. 271(29),pp. 17547-17554]. The Examiner asserts that the anti-rabbit eEF-2 antibodies of Redpath et al., which react with rat eEF-2 Kinase, would react with the disclosed sequences. The Examiner further asserts that "specifically binding" is generally taken to mean binding that is saturable and computable. Applicants respectfully disagree and submit that antibodies raised against the rabbit eEF-2 kinase do not anticipate per se the claimed antibodies specifically binding to human eEF-2 kinase, specifically binding to mouse eEF-2 kinase protein, or specifically binding to C. elegans eEF-2 kinase protein. The claimed antibodies immunoreact with the human, mouse or C. elegans eEF-2 kinase, but do not react with a non-human, non-mouse or non-C. elegans eEF-2 kinase. Thus an antibody specifically binding to the human eEF-2 kinase and not immunoreacting with a non-human eEF-2 kinase, for instance rat eEF-2 kinase or rabbit eEF-2 kinase is claimed. The antibodies as claimed specifically bind to the noted eEF-2 kinase and are clearly distinct from the

antibodies of Redpath et al. Redpath does not disclose or suggest the particular eEF-2 kinase sequences of the instant Application and further does not disclose or suggest the specific antibodies thereto. Applicants cannot and do not assert whether the antibodies of Redpath would bind to human or mouse eEF-2 kinase. Applicants, however, do assert that antibodies specific for the human eEF-2 kinase, and not immunoreacting with the rat or rabbit eEF-2 kinase can be made by the skilled artisan and claim these antibodies.

In view of the foregoing remarks and amendments, Applicants submit that the Examiner's rejections under 35 U.S.C. § 102 are overcome and should be withdrawn.

The §103 Rejections

The Examiner has maintained her rejection of Claim 51 and 53-59 under 35 U.S.C. § 103(a) as unpatentable over Redpath et al. [J. Biol. Chem. 1996, Vol. 271(29), pp. 17547-17554], in view of Harlow and Lane, Antibodies, 1988. Applicants again argue that Redpath does not disclose or suggest the particular eEF-2 kinase sequences of the instant Application and further does not disclose or suggest the specific antibodies thereto. The knowledge of how to make antibodies in general, as provided by Harlow and Lane, does not make any and all antibodies to any sequence obvious per se - including labeled antibodies, antibody fragments, and pharmaceutical compositions comprising said antibodies - as suggested by the Examiner, particularly wherein the sequence of the protein to which the antibody is specifically directed is not disclosed or known. More particularly, wherein differences in amino acid sequence between the new and novel sequence and known protein sequence exist, the previously known antibodies do not make specific antibodies directed against and immunoreactive with the new and novel protein sequence obvious. Applicants claim antibodies which specifically bind the human, mouse or C. elegans eEF-2 kinase of Applicants, wherein these specific antibodies are not immunoreactive with the previously known non-human, non-mouse and non-C. elegans eEF-2 kinase. Thus, these antibodies specifically bind the eEF-2 kinases disclosed and taught by Applicants. The making and testing of these specific antibodies are well within the knowledge and capability of the skilled artisan. In particular, Applicants point out that many amino acid sequence differences exist, for example, between the human and rat eEF-2 kinase, as

demonstrated by a BLAST comparison of the two amino acid sequences (attached as Exhibit A). A review of the BLAST results clearly demonstrates amino acid differences, and particularly regions or peptides wherein a significant number of differences exist in a short stretch of amino acids. These amino acids would readily be recognized by the skilled artisan as ones to utilize or target in making and isolating specific binding antibodies thereto.

In a further 103 rejection, the Examiner maintains her rejection of Claims 51-59 under 35 U.S.C. 103(a) as unpatentable over Ryazanov et al [PNAS May 1997, vol. 94, pp. 4884-4889] in view of Harlow and Lane. Applicants again point out that Ryazanov et al, which indicates all of the inventors of the present application as authors, and the entire disclosure of which is included in the instant Specification, was published less than one year prior to the date of filing (August 20, 1997) of the instant Application and is therefore also not appropriate as a prior art reference. Applicants provide herewith a Katz-type declaration by inventor Alexey Ryazanov clarifying that Applicant Ryazanov et al. (1997) describes his work and any additional authors are not inventors. In as much as Ryazanov et al is not a true prior art reference, it cannot make obvious the antibodies in combination with Harlow and Lane.

In view of the foregoing remarks and amendments, Applicants submit that the Examiner's rejections under 35 U.S.C. § 103 are overcome and should be withdrawn.

The Specification Enables the Claimed Invention and the Claims are Definite

The Examiner has maintained her rejection of Claim 59 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the Specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. The Examiner again asserts that it would require undue experimentation to use the antibodies as pharmaceutical compositions. Applicants respectfully disagree and submit that the Specification clearly enables the skilled artisan to make and/or use a pharmaceutical composition comprising an eEF-2 antibody. While some experimentation to make and test such pharmaceutical compositions would be necessary, such experimentation would utilize well known methods and standard skills and would <u>not</u> constitute <u>undue</u> experimentation. The Examiner particularly and correctly points out that Applicants have taught evidence of upregulation of eEF-2 kinase in

cancers and diagnostic use of the antibodies. In view of the foregoing, Applicants submit that given the guidance provided by the specification, the well known criteria or parameters for making and testing of antibodies, and the significant level of skill in the art a person of ordinary skill in the art could, without undue experimentation, make and use the pharmaceutical compositions encompassed by the claims.

The Examiner rejects Claim 58 under 35 U.S.C. 112, second paragraph, as being indefinite in the term "active fragment" of an antibody. The Examiner asserts that there is no definition of what activity the fragment is required to have and the claim is therefore indefinite. Applicants argue that the skilled artisan would readily understand that an active fragment of an eEF-2 antibody is one capable of binding to or immunoreacting with the kinase. Applicants have above amended Claim 58 to clarify that the active fragment specifically binds to the particular eEF-2 kinase of SEQ ID NO:2, 4 or 10.

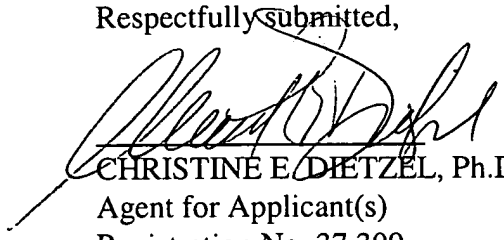
The Examiner newly rejects claims 51-59 under 35 U.S.C., second paragraph, as being indefinite in the recitation of "specifically binds". The Examiner asserts that the skilled artisan would not know what degree of binding was considered to be specific. Applicants respectfully disagree and again assert that the term "specifically binds" is recognized by the skilled artisan to mean specific binding to and/or specific recognition of an epitope. Applicants have above amended claims 51, 52, 53, 54, 55, 57 and 59 to more particularly point out the claimed invention. Applicants claim antibodies which specifically bind the human, mouse or C. elegans eEF-2 kinase of Applicants, wherein these specific antibodies are not immunoreactive with the previously known non-human, non-mouse and non-C. elegans eEF-2 kinase. Thus, these antibodies specifically bind the eEF-2 kinases disclosed and taught by Applicants. Applicants assert that the skilled artisan would readily understand the meaning and intent of "specifically binds", particularly as now claimed.

In view of the foregoing remarks, Applicants submit that the Examiner's rejection under 35 U.S.C.§ 112, first paragraph and second paragraph, are overcome and should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,



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Complete Listing of Claims in Application U.S.S.N. 09/994,485

Claims 1-49 (canceled)

Claim 50 (canceled)

51. (currently amended) An isolated antibody which specifically binds to a human, mouse or C. elegans eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10, wherein said antibody does not immunoreact with a non-human, non-mouse or non-C. elegans eukaryotic eEF-2 kinase.

52. (currently amended) An isolated antibody which specifically binds to a human eEF-2 kinase capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising the amino acid sequence of SEQ ID NO:2, wherein said antibody does not immunoreact with a non-human eukaryotic eEF-2 kinase.

53. (currently amended) A monoclonal antibody which specifically binds to a human, mouse or C. elegans eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10, wherein said antibody does not immunoreact with a non-human, non-mouse or non-C. elegans eukaryotic eEF-2 kinase.

54. (currently amended) An immortal cell line that produces a monoclonal antibody which specifically binds to a human, mouse or C. elegans eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the

group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10, wherein said antibody does not immunoreact with a non-human, non-mouse or non-C. elegans eukaryotic eEF-2 kinase.

55. (currently amended) An isolated antibody which specifically binds to a human, mouse or C. elegans eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10, said antibody labeled with a detectable label, wherein said antibody does not immunoreact with a non-human, non-mouse or non-C. elegans eukaryotic eEF-2 kinase.

56. (previously amended) The antibody of Claim 55 wherein the label is selected from enzymes, chemicals which fluoresce and radioactive elements.

57. (currently amended) A radioactively labeled antibody which specifically binds to a human, mouse or C. elegans eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10, wherein said antibody does not immunoreact with a non-human, non-mouse or non-C. elegans eukaryotic eEF-2 kinase.

58. (currently amended) An active fragment of an isolated antibody which specifically binds to a human, mouse or C. elegans eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said active fragment specifically binding to said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10, said active fragment selected from the group of Fab, Fab', $F(ab')_2$ and Fv fragments, wherein said active fragment does not immunoreact with a non-human, non-mouse or non-C. elegans eukaryotic eEF-2 kinase.

59. (currently amended) A pharmaceutical composition comprising:

A. a therapeutically effective amount of an antibody which specifically binds to a human, mouse or C. elegans eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10, or an active fragment of said antibody, wherein said antibody or said active fragment does not immunoreact with a non-human, non-mouse or non-C. elegans eukaryotic eEF-2 kinase; and,

B. a pharmaceutically acceptable carrier.

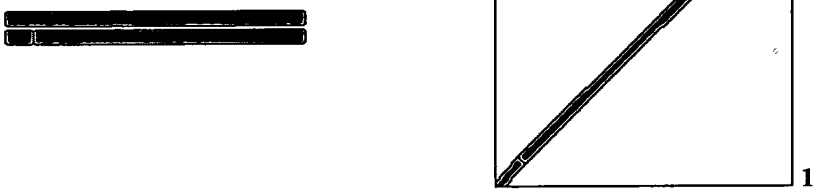
Blast 2 Sequences results

BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.6 [Apr-09-2003]

Matrix BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.00 wordsize: 3 Filter Align

Sequence 1 lcl|human eEF-2 kinase **Length** 725 (1 .. 725)

Sequence 2 lcl|rat eEF-2 kinase **Length** 724 (1 .. 724)



NOTE:The statistics (bitscore and expect value) is calculated based on the size of nr database

Score = 1355 bits (3508), Expect = 0.0
Identities = 655/725 (90%), Positives = 685/725 (94%), Gaps = 1/725 (0%)

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Sbjct: 1   MADEDLIFRLEGVDGGGSSGAGRHGDSDTDSDDDEGYFICPITDDHMSNQNVNSKGQGYY 60

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           +NL K+E   S+GSPA+SFHFKEAWKHAI+KAKHMPDPWAEFHLEDIATE ATRHRYNAV
Sbjct: 61  NNLLKTE-CGSTGSPASSFHFKEAWKHAIEKAKHMPDPWAEFHLEDIATEHATRHRYNAV 119

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Sbjct: 360 RIRTLSGSRPPLLLRLSENSGDENMSDVTFDSLPSSPSSATPHSQKLDHLHWPVFGDLDN 419

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Gapped
Lambda     K      H
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S1: 41 (21.6 bits)
S2: 79 (35.0 bits)
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